

**AMENDMENTS TO THE SPECIFICATION:**

*On page 1, after the title, please insert the following new paragraph as follows:*

This application is a National Stage Application of PCT/JP2003/010449, filed August 19, 2003 and claims priority from Japanese Patent Application No. 2002-382083, filed November 24, 2002, which is incorporated herein by reference in its entirety.

*Please amend paragraph [0088] as follows:*

[0088] Cell morphology was examined as follows. ~~Infected cells~~ Cells were planted in 12-well tissue culture plates to get  $3.0 \times 10^4$  cells per well. After 3 h of incubation at 37 °C, cells were infected with adenoviruses (multiplicity of infection (MOI) = 200), cultured for a further 36 h and then observed by a phase-contrast microscope. Cells infected with AdAsef- $\Delta$ APC became flattened onto the substratum and exhibited membrane ruffles and lamellipodia. In contrast, cells infected with AdAsef- $\Delta$ DH showed no morphological changes and resembled uninfected cells:

*Please amend paragraph [0092] as follows:*

[0092] Cells infected with a plasmid that contains DNA encoding Asef-full showed enhanced motility as compared with parental cells (MDCK) or vector-transfected cells (Mock) (Figure 2). Cells that were made to co-express the Asef-full gene together with any one of the APC-arm gene, the APC-876 gene and the APC-1309 gene were more motile than cells transfected with the Asef-full gene alone. In the effect of APC on the ability of Asef to promote cell-motility, APC-arm, APC-876 and APC-1309 were stronger than APC-full. In contrast, APC-arm alone did not promote migration. In addition, cells transfected with the Asef- $\Delta$ APC gene showed a further enhanced migration reaction as compared with cells cotransfected with the

Asef-full gene and the APC-arm gene. These results showed that Asef has the potential to promote the migration of MDCK cells. It was shown that this potential of Asef is further enhanced by APC, particularly a truncated APC mutant that contains an armadillo repeat domain (~~Asef-Arm~~) (APC-Arm). In addition, Asef- $\Delta$ HD did not promote the migration of MDCK cells, indicating that the GEF activity of Asef is required for such migration stimulatory activity.

*Please amend paragraph [0092] as follows:*

[0094] Next, the motility of SW480 cells that are known to include Asef and truncated APC mutants was examined. When SW480 cells were transfected with plasmids that contain DNA encoding Asef-ABR, the migration of the cells decreased to about 50% of that of the parental cells or Mock cells (Figure 2). Similarly, the migration of SW480 cells transfected with Asef- $\Delta$ HD plasmids decreased ~~by~~ to about 40%. These results demonstrated that Asef-ABR or Asef- $\Delta$ HD expressed in cells acts on the binding of Asef to truncated APC mutants in a dominant-negative manner, thereby inhibiting the cell migration ~~by Asef-ABR or Asef- $\Delta$ HD~~.